REMARKS/ARGUMENTS

The examiner is thanked for numerous helpful comments which have better defined the issues remaining to be addressed.

In response to the objection to claim 35, claim 35 has been made dependent from pending claim 22.

In response to the indefiniteness rejection, all rejected claims have been amended to address the language to which the Examiner objected, except prodrugs were retained for the following reasons. Prodrugs are well-defined in the art as a class of agents that deliver a given active ingredient through *in vivo* conversion following administration. It is rare in the pharmaceutical industry that the particular active ingredient that is to be delivered to the bloodstream of a patient is not formulated (in its dosage form) as some form of prodrug which is a physiologically inactive compound which is converted *in vivo* to the desired active compound by a well-known mechanism. For example, a large percentage of pharmaceutical active ingredients are packaged by pharmaceutical companies in the form of acid salts, *e.g.*, hydrochloric acid salts, which simply dissociate into the desired active compound as soon as introduced into an aqueous environment. Likewise, it is common in the industry to change hydroxy groups of active compounds, such as those utilized herein, into (for example) ester groups which are then converted back to the desired hydroxy group of the active compound *in vivo*. We enclose excerpts from *A Textbook of Drug Design and Development*, (Bundgaard and Larsen, 1991) (hereafter "Prodrug Handbook") which show other well-known prodrug forms of various functional groups that may appear on the active compound that is to be delivered. Pharmaceutical companies may prefer these prodrug forms for a number of reasons unrelated to biological function of the active ingredient. These reasons may include ease of manufacture, shelf stability, crystallinity, easier synthesis purification, etc.

It is believed that the present specification provides sufficient support for reciting the genus of "prodrugs" of its small number of recited active compounds, for the following reasons:

(1) The term "prodrug" is not broad in any practical sense. It does not cover an undefined universe of compounds. It covers only those compounds which deliver,

to the bloodstream of a patient, one of the small number of active ingredients recited in the body of the claim.

(2) The term "prodrug" does not broadly cover compounds that would not be expected to work in the context of the invention. If the recited active compounds work, then obviously any prodrug which delivers one of the same active compounds must *ipso facto* work also.

For all of the foregoing reasons, it is urged that the rejection for indefiniteness be withdrawn.

In response to the double-patenting rejection, a terminal disclaimer is enclosed herewith. Accordingly, the double patenting rejection should be withdrawn.

In response to the two anticipation rejections over (1) Simard and (2) Couillard, note that all claims require estrogen while both Simard and Couillard teach against estrogen. Couillard notes at abstract lines 6-7, "Estrone caused a 10-fold increase in ZR-75-1 tumor area . . ." ZR-75-1 is defined as human mammary tumor. Likewise, Simard states that "estrogens play a predominant role in the development and growth of human breast cancer . . ." (Abstract, lines 1-2). Accordingly, it is urged that the anticipation rejection should be withdrawn. For the same reason, the related obviousness rejection should be withdrawn.

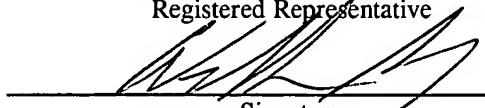
Regarding the final obviousness rejection, the examiner indicates (page 11 of the office action) that applicants' prior arguments were not pursuasive because although DHEA is not an estrogen, the claims (written with "comprising" transition) do not exclude DHEA. While it is true that the claims do not exclude DHEA, the claims require estrogen. References which teach DHEA, but not estrogen, cannot provide this important requirement of the claims. Accordingly, it is urged that the obviousness rejection be withdrawn.

It is believed that the application is now in condition for allowance. Issuance of a notice of allowance is requested.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on August 8, 2005:

William O. Gray, III

Name of applicant, assignee or Registered Representative



Signature

August 8, 2005

Date of Signature

Respectfully submitted,

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A Textbook of DRUG DESIGN and DEVELOPMENT

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The Royal Danish School of Pharmacy
Copenhagen, Denmark

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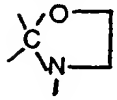
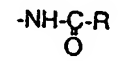
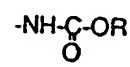
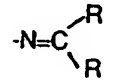
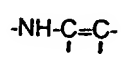
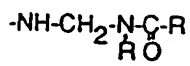
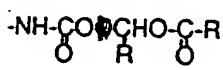
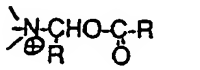
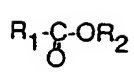
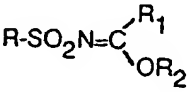
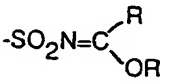
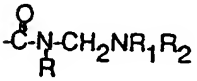
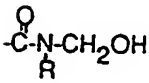
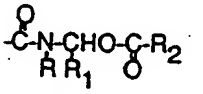
Table 5.5 Prodrug forms of various functional groups in drug substances.

Functional group	Prodrug form	
-COOH	-COOR	Esters
	-COOCHOOCR R	α-Acyloxyalkyl esters
	-CONHR	Amides
-OH	-OOCR	Esters
	-OCOR O	Carbonate esters
	-O-P(OH)(=O)-OH	Phosphate esters
	-OR	Ethers
	-OCHOOCR R	α-Acyloxyalkyl ethers
-SH	-SCR O	Thioesters
	-SCHOOCR R	α-Acyloxyalkyl thioethers
	-S-S-R	Disulphides
>C=O	-C(OR)(OR)-	Ketals
	>C=N-R	Imines
	>C-OOCR	Enol esters
		Oxazolidines
		Thiazolidines

(continued)

Table 5.5 (continued)

Functional group	Prodrug form	
$-NH_2$		Amides
		Carbamates
		Imines
		Enamines
		N-Mannich bases
		N-Acyloxyalkoxycarbonyl derivatives
		N-Acyloxyalkyl derivatives
		N-Sulphonyl imidates
$-SO_2NH_2$		N-Sulphonyl imidates
	$-SO_2NH-CH_2OR$	N-Alkoxymethyl derivatives
NH-Acidic group		N-Mannich bases
e.g. 		N-Methylols
or heterocyclic amine		N-Acyloxyalkyl derivatives

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(continued)